



General

Guideline Title

Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society.

Bibliographic Source(s)

Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012 Apr 24;78(17):1337-45. [40 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000 Sep 26;55(6):754-62.

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Recommendations

Level A. The following medications are established as effective and should be offered for migraine prevention:

- Antiepileptic drugs (AEDs): divalproex sodium, sodium valproate, topiramate
- Beta-blockers: metoprolol, propranolol, timolol
- Triptans: frovatriptan for short-term menstrually associated migraine (MAMs) prevention

Level B. The following medications are probably effective and should be considered for migraine prevention:

- Antidepressants: amitriptyline, venlafaxine
- Beta-blockers: atenolol, nadolol
- Triptans: naratriptan, zolmitriptan for short-term MAMs prevention

Level C. The following medications are possibly effective and may be considered for migraine prevention:

- Angiotensin-converting enzyme (ACE) inhibitors: lisinopril
- Angiotensin receptor blockers: candesartan
- Alpha-adrenoceptor agonists: clonidine, guanfacine
- AEDs: carbamazepine
- Beta-blockers: nebivolol, pindolol

Level U. Evidence is conflicting or inadequate to support or refute the use of the following medications for migraine prevention:

- AEDs: gabapentin
- Antidepressants
 - Selective serotonin reuptake inhibitor/selective serotonin-norepinephrine reuptake inhibitors: fluoxetine, fluoxamine
 - Tricyclics: protriptyline
- Antithrombotics: acenocoumarol, Coumadin, picotamide
- Beta-blockers: bisoprolol
- Calcium-channel blockers: nicardipine, nifedipine, nimodipine, verapamil
- Acetazolamide
- Cyclandelate

Level A negative. The following medication is established as ineffective and should not be offered for migraine prevention:

• Lamotrigine

Level B negative. The following medication is probably ineffective and should not be considered for migraine prevention:

Clomipramine

Level C negative. The following medications are possibly ineffective and may not be considered for migraine prevention:

- Acebutolol
- Clonazepam
- Nabumetone
- Oxcarbazepine
- Telmisartan

Clinical Context

Evidence to support pharmacologic treatment strategies for migraine prevention indicates which treatments might be effective but is insufficient to establish how to choose an optimal therapy. Consequently, although Level A recommendations can be made for pharmacologic migraine prevention, similar evidence is unavailable to help the practitioner choose one therapy over another. Treatment regimens, therefore, need to be designed case by case, which may include complex or even nontraditional approaches. Moreover, decision-making must remain with the physician and the patient to determine the optimal therapy, accounting for efficacy, adverse effects, coexisting/comorbid conditions, and personal considerations. Often trial and error is needed.

Evidence is also unavailable for making broad-range comparisons among multiple agents within a single class; such evidence would provide a more comprehensive understanding of relative efficacy and tolerability profiles across a broader range of therapeutic agents. Studies are needed that specifically evaluate when preventive therapy is warranted and how medications should be titrated. Table e-1 of the data supplement (see the "Availability of Companion Documents" field) lists some specific consensus-based clinical circumstances wherein considering preventive therapy would be reasonable. A shortcoming of migraine prevention clinical studies is the relatively brief treatment duration (often only 12–16 weeks). Long-term assessment of the efficacy and safety of migraine preventive treatments is needed. Additionally, overall cost is a consideration when prescribing medications; cost may influence compliance, especially long-term

It seems reasonable that a clinician be mindful of comorbid and coexistent conditions in patients with migraine, to maximize potential treatment efficacy and minimize adverse effect risk. Table e-2 of the data supplement (see the "Availability of Companion Documents" field) identifies which therapies to consider or avoid when common migraine coexisting conditions are present. Because migraine is frequent in women of childbearing age, the potential for adverse fetal effects related to migraine prevention strategies is particularly concerning.

Evidence from the 2 Class I frovatriptan studies meets the American Academy of Neurology (AAN) threshold for a Level A recommendation for short-term use to prevent menstrual migraine (reduction in MAM headache incidence by 26% on 2.5 mg BID). However, the Food and Drug

Administration questions whether the benefit demonstrated is clinically meaningful and has not approved frovatriptan for this indication.

Definitions:

Classification of Recommendations

Level A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*

Level B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting, given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Classification of Evidence for Rating of a Therapeutic Article

Class I = A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined
- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and cross-overs with numbers sufficiently low to have minimal potential for bias
- e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
 - 1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.
 - 2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
 - 3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
 - 4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II = A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a—e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b—e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III = All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.**

Class IV = Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Clinical Algorithm(s)

Scope

Disease/Condition(s)

Migraine headache, including menstrual-associated migraine (MAM)

Guideline Category

Assessment of Therapeutic Effectiveness

Prevention

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Neurology

Preventive Medicine

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide updated evidence-based recommendations for the preventive treatment of migraine headache with effective pharmacologic therapies
- To review the safety and efficacy of pharmacologic therapies for migraine prevention

Target Population

Adults with migraine headaches, including menstrual associated migraine (MAM)

Interventions and Practices Considered

- 1. Antiepileptic drugs (AEDs): divalproex sodium, sodium valproate, topiramate, carbamazepine
- 2. Beta-blockers: metoprolol, propranolol, timolol, atenolol, nadolol, nebivolol, pindolol
- 3. Triptans: frovatriptan, naratriptan, zolmitriptan for short-term menstrually associated migraine (MAMs) prevention
- 4. Antidepressants: amitriptyline, venlafaxine

- 5. Angiotensin-converting enzyme (ACE) inhibitors: lisinopril
- 6. Angiotensin receptor blockers: candesartan
- 7. Alpha-adrenoceptor agonists: clonidine, guanfacine

Note: Evidence is conflicting or inadequate to support or refute the use of the following medications for migraine prevention: gabapentin, fluoxetine, fluoxamine, protriptyline, acenocoumarol, Coumadin, picotamide, bisoprolol, nicardipine, nifedipine, nimodipine, verapamil, acetazolamide, cyclandelate. Lamotrigine is established as ineffective and should not be offered for migraine prevention. Clomipramine is probably ineffective and should not be considered for migraine prevention. The following medications are possibly ineffective and may not be considered for migraine prevention: acebutolol, clonazepam, nabumetone, oxcarbazepine, telmisartan.

Major Outcomes Considered

- Migraine attack frequency
- Number of migraine days
- Attack severity
- Migraine-free perimenstrual periods (PMPs)

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Computerized searches of the MEDLINE, PsycINFO, and CINAHL databases identified new studies (published in English). The search strategy used the MeSH term "headache" (exploded) and a published search strategy for identifying randomized controlled trials (RCTs) published between June 1999 and May 2007. Additional MEDLINE searches revealed studies published through May 2009, which were reviewed and included as supplemental articles.

Studies of pharmacologic agents available in the United States were included in the analysis if they randomized adult patients with migraine to the agent under study or a comparator drug (including placebo) and utilized masked outcome assessment.

Studies were excluded if they:

- Assessed the efficacy of therapeutic agents for headache other than episodic migraine in adults
- Assessed acute migraine treatment, migraine aura treatment/prevention, or nonpharmacologic treatments (e.g., behavioral approaches)
- Used quality of life measures, disability assessment, or nonstandardized outcomes as primary efficacy endpoints
- Tested the efficacy of drugs not available in the United States

Number of Source Documents

The original search identified 179 articles. A supplemental search (2007–2009) yielded 105 additional articles. Of the total 284 articles, 29 were classified as Class I or Class II and were reviewed.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of Evidence for Rating of a Therapeutic Article

Class I = A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required:

- a. Concealed allocation
- b. Primary outcome(s) clearly defined
- c. Exclusion/inclusion criteria clearly defined
- d. Adequate accounting for drop-outs (with at least 80% of enrolled subjects completing the study) and cross-overs with numbers sufficiently low to have minimal potential for bias
- e. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
 - 1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority.
 - 2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective).
 - 3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment.
 - 4. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Class II = A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria a—e above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets b—e above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Class III = All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.**

Class IV = Studies not meeting Class I, II, or III criteria including consensus or expert opinion.

*Note that numbers 1-3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

At least 2 panelists independently reviewed each study and rated it according to the American Academy of Neurology (AAN) therapeutic classification of evidence scheme (see the "Rating Scheme for the Strength of the Evidence" field). Differences in ratings were resolved by author panel discussion.

Since the 2000 guideline publication, the AAN revised its evidence classification criteria to include study completion rates. Studies with completion rates below 80% were downgraded; several studies in the original guideline have thus been downgraded.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The American Academy of Neurology (AAN) and the American Headache Society participated in the development process. An author panel of headache and methodologic experts was assembled to review the evidence.

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

A = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*

B = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

C = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Drafts of the guidelines have been reviewed by at least three American Academy of Neurology (AAN) and American Headache Society (AHS) committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The guidelines were approved by the Quality Standards Subcommittee on February 19, 2011; by the Practice Committee on June 19, 2011; by the American Headache Society (AHS) Board of Directors on March 29, 2012; and by the American Academy of Neurology (AAN) Board of Directors on January 27, 2012.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

No new Class I or II studies were published for acebutolol, atenolol, bisoprolol, carbamazepine, clonazepam, clonidine, clomipramine, fluvoxamine, guanfacine, nabumetone, nadolol, nicardipine, nifedipine, or protriptyline. Recommendations for these agents are based on the evidence reviewed in the original guideline (see table 1 of the guideline document). Currently, no Class I or Class II studies exist for anticoagulants (limited Class III and IV studies were identified; table 1 includes anticoagulants).

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Prevention of migraine attacks, including menstrual-related migraines (MAMs) through appropriate pharmacologic therapy

Potential Harms

- Adverse effects of pharmacologic therapies (refer to the original guideline for drug-specific information)
- It seems reasonable that a clinician be mindful of comorbid and coexistent conditions in patients with migraine, to maximize potential treatment efficacy and minimize adverse effect risk. Table e-2 of the data supplement (see the "Availability of Companion Documents" field) identifies which therapies to consider or avoid when common migraine coexisting conditions are present. Because migraine is frequent in women of childbearing age, the potential for adverse fetal effects related to migraine prevention strategies is particularly concerning.

Qualifying Statements

Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology (AAN) and the American Headache Society (AHS). It is based on as assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN and the AHS recognize that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. No formal practice recommendations should be inferred.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

Staff Training/Competency Material

For information about availability, see the Availability of Companion Documents and Patient Resources fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults: report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012 Apr 24;78(17):1337-45. [40 references] PubMed

Adaptation

Not applicable: Guideline was not adapted from another source.

Date Released

2000 Sep (revised 2012 Apr 24)

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

American Headache Society - Professional Association

Source(s) of Funding

This guideline was developed with financial support from the American Academy of Neurology and the American Headache Society. None of the authors received reimbursement, honoraria, or stipends for their participation in development of this guideline.

Guideline Committee

Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society

Composition of Group That Authored the Guideline

Guideline Authors: S.D. Silberstein, MD, FACP; S. Holland, PhD; F. Freitag, DO; D.W. Dodick, MD; C. Argoff, MD; E. Ashman, MD

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Financial Disclosures/Conflicts of Interest

Conflict of Interest

The American Academy of Neurology (AAN) and the American Headache Society (AHS) are committed to producing independent, critical and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN and AHS keep separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN and AHS limit the participation of authors with substantial conflicts of interest. The AAN and AHS forbid commercial participation in, or funding of, guideline projects. Drafts of the guidelines have been reviewed by at least three AAN and AHS committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at the American Academy of Neurology website

Disclosure

Dr. Silberstein is on the advisory panel of and receives honoraria from AGA, Allergan, Amgen, Capnia, Coherex, Colucid, Cydex, GlaxoSmithKline, Lilly, MAP, Medtronic, Merck, Minster, Neuralieve, NINDS, NuPathe, Pfizer, St. Jude Medical, and Valeant. He is on the speakers' bureau of and receives honoraria from Endo Pharmaceuticals, GlaxoSmithKline, and Merck. He serves as a consultant for and receives honoraria from Amgen and Novartis. His employer receives research support from AGA, Allergan, Boston Scientific, Capnia, Coherex, Endo Pharmaceuticals, GlaxoSmithKline, Lilly, MAP, Medtronic, Merck, NINDS, NuPathe, St. Jude Medical, and Valeant Pharmaceuticals. Dr. Holland (formerly Dr. Pearlman) receives consulting income from Map Pharmaceuticals and the American Headache Society and research support from Albert Einstein College of Medicine. Dr. Freitag has served on the scientific advisory boards of Zogenix Pharmaceuticals, Allergan Pharmaceuticals, Nautilus, MAP Pharmaceuticals, and Nupathe; has received travel expenses and or honoraria from GlaxoSmithKline, Zogenix, Merck, Nautilus, Allergan, Diamond Headache Clinic Research and Educational Foundation (not for profit), and the American Headache Society (travel). Dr. Freitag is a member of the Board of Directors of the National Headache Foundation. Dr. Dodick, within the past 3 years, serves on advisory boards and has consulted for Allergan, Alder, Pfizer, Merck, Coherex, Ferring, Neurocore, Neuralieve, Neuraxon, NuPathe Inc., MAP, SmithKlineBeecham, Boston Scientific, Medtronic, Inc., Nautilus, Eli Lilly & Company, Novartis, Colucid, GlaxoSmithKline, Autonomic Technologies, MAP Pharmaceuticals, Inc., Zogenix, Inc., Impax Laboratories, Inc., Bristol Myers Squibb, Nevro Corporation, Atlas, Arteaus, and Alder Pharmaceuticals. Within the past 3 years, Dr. Dodick has received funding for travel, speaking, or editorial activities from CogniMed, Scientiae, Intramed, SAGE Publishing, Lippincott Williams & Wilkins, Oxford University Press, Cambridge University Press, Miller Medical, Annenberg for Health Sciences; he serves as Editor-in-Chief and on the editorial boards of *The Neurologist*, *Lancet Neurology*, and Postgraduate Medicine; and has served as Editor-in-Chief of Headache Currents and as an Associate Editor of Headache; he receives publishing royalties for Wolff's Headache, 8th edition (Oxford University Press, 2009) and Handbook of Headache (Cambridge University Press, 2010). Within the past 3 years, Dr. Dodick has received research grant support from Advanced Neurostimulation Systems, Boston Scientific, St Jude Medical, Inc., Medtronic, NINDS/NIH, Mayo Clinic. Dr. Argoff has served on a scientific advisory board for the Department of Defense and DSMB for the NIH; has received funding for travel and/or speaking and/or has served on a speakers' bureau for Pfizer (King), Janssen (Pricara), Millennium Laboratories, Neurogesx, Forest Laboratories, Eli Lilly, Covidien, and Endo Pharmaceuticals; has received research support from Endo Pharmaceuticals, Forest Laboratories, Eli Lilly, Neurogesx, Pfizer, and SBRT funded by the NIH; and has received stock/stock options from Pfizer. Dr. Ashman is the Level of Evidence editor for Neurology and serves on the AAN Guideline Development Subcommittee. He reports no other disclosures. Full disclosures were provided at the time of Board approval. Full disclosures are provided at neurology.org

Guideline Endorser(s)

American Osteopathic Association - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidencebased review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2000 Sep 26;55(6):754-62.

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Patient Resources

The following is available:

• Pharmacologic treatment of episodic migraine prevention in adults. AAN summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology. 2012. 2 p. Electronic copies: Available in English and in Portable Document Format (PDF) from the American Academy of Neurology (AAN) Web site. Spanish

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI on February 12, 2002. The information was verified by the guideline developer on September 5, 2003. This summary was updated by ECRI on January 12, 2005 following the release of a public health advisory from the U.S. Food and Drug Administration regarding the use of some non-steroidal anti-inflammatory drug products. This summary was updated on April 15, 2005 following the withdrawal of Bextra (valdecoxib) from the market and the release of heightened warnings for Celebrex (celecoxib) and other nonselective nonsteroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on June 16, 2005, following the U.S. Food and Drug Administration advisory on COX-2 selective and non-selective non-steroidal anti-inflammatory drugs (NSAIDs). This summary was updated by ECRI on October 3, 2005, following the U.S. Food and Drug Administration advisory on Paxil (paroxetine). This summary was updated by ECRI on December 12, 2005, following the U.S. Food and Drug Administration advisory on Paroxetine HCL - Paxil and generic paroxetine. This NGC summary was updated by ECRI Institute on June 29, 2012. This summary was updated by ECRI Institute on July 10, 2013 following the U.S. Food and Drug Administration advisory on Valproate.

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